REMARKS

Claims 1-5, 8, 10, 21-31, and 37-46 were pending in the subject application. The Examiner indicated that claims 4, 40, 45, and 46 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Such amendment has been done as described below.

Claims 21-31 were withdrawn from consideration by the Examiner as drawn to a non-elected invention. By this Amendment, claims 21-31 have been canceled without prejudice or disclaimer, claims 4 and 40 have been amended, and new claims 47-51 have been added. Accordingly, upon entry of this Amendment, claims 1-5, 8, 10, and 37-51 will be pending and under consideration.

Applicants maintain that the amendments to claims 4 and 40, and the addition of new claims 47-51 do not raise an issue of new matter. Support for the amendment to claim 4 can be found at least in claim 1. Support for the amendment to claim 40 can be found at least in claim 37. Support for new claims 47 and 48 can be found *inter alia* in the specification at least on page 14, line 10, through page 16, line 17. Support for new claim 49 can be found *inter alia* in the specification at least on page 14, line 10, through page 16, line 17, and in claim 1. Support for new claim 50 can be found in claims 1 and 3. Support for new claim 51 can be found in claims 37 and 38. Accordingly, entry of the amendment is respectfully requested.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 1, 37, 42, and 43 are rejected under 35 U.S.C. §112, first paragraph. The Examiner indicated that the specification, while being enabling for β-agonists recited in claim 2, does not reasonably provide enablement for other suitable β-agonists.

Applicants thank the Examiner for the indication of enablement for agonists

recited in claim 2. However, applicants respectfully traverse this rejection.

Applicants note that the claimed invention is not directed to the use of all β-agonists, rather the invention as set forth in the pending claims is specifically directed to use of β_2 adrenergic agonists (see also, e.g., specification, page 7, lines 8-10).

Methods to distinguish β_2 agonists from other compounds that act at β adrenergic receptors are known in the art and described in the specification, for example, on page 6, lines 4-10, and on page 7, line 11, through page 8, line 4.

Examples of β_2 agonists are provided in the specification on page 6, line 11, through page 7, line 7.

Appropriate doses of administration of β_2 agonists are discussed on page 8, line 10, through page 9, line 8.

Finally, in addition to working examples for the β_2 agonist clenbuterol, to which the Examiner refers, the specification further provides working examples for the β_2 agonist salbutamol (see page 17, lines 10-23, and Figure 9).

Accordingly, applicants maintain that the teachings of the specification enable the skilled artisan to practice the claimed invention without undue experimentation.

In view of the remarks made hereinabove, reconsideration and withdrawal of this ground of rejection are respectfully requested.

Rejections under 35 U.S.C. §112, Second Paragraph

Claims 2-3 and 38-39 are rejected under 35 U.S.C. §112, second paragraph, because the claims recite "BRL-47672", "MJ-9184-1", "QH-25" and "R-804". The Examiner indicated that the claim scope is uncertain because a trade name cannot be used to properly identify any particular material.

Applicants respectfully traverse this rejection.

The terms BRL-47672, MJ-9184-1, QH-25 and R-804 designate specific compounds known in the art. As an example, the chemical structures of MJ-9184-1, QH-25 and R-804 are illustrated in Figure 3A in U.S. Patent No. 6,015,837, a copy of which is attached hereto. Furthermore, the claims of U.S. Patent No. 6,015,837, which are presumed valid, recite BRL-47672, MJ-9184-1, QH-25 and R-804. U.S. Patent No. 6,015,837 is incorporated by reference into the subject application (see page 6, lines 9-10).

Accordingly, in view of the remarks made hereinabove, reconsideration and withdrawal of this ground of rejection are respectfully requested.

Rejections under 35 U.S.C. §102

Claims 1-3, 5, 8, 37-39 and 41-44 are rejected under 35 U.S.C. §102(a) as being anticipated by Murphy et al. (Arch. Phys. Med. Rehabil. 80(10): 1264-67, 1999).

Claims 1-3, 5, 37-39 and 41 are rejected under 35 U.S.C. §102(b) as being anticipated by Vaidyanathan et al. (Spinal Cord 34: 691-695, 1996).

Applicants respectfully traverse these rejections.

Applicants note that "[a] single prior art reference anticipates a patent claim if it expressly or inherently describes each and every limitation set forth in the patent claim. *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Inherent anticipation requires that the missing descriptive material is "necessarily present," not merely probably or possibly present, in the prior art. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citing *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746,

1749 (Fed. Cir. 1991))." *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295, 63 USPQ2d 1597, 1599 (Fed. Cir. 1992).

Applicants further note that:

> A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed.Cir.1990). In addition, the reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. *Id. In re Paulsen*, 30 F.3d 1475, 1478-1479, 31 USPQ 2d 1671, 1673 (Fed. Cir.1994).

Murphy et al. teach that administration of salbutamol to paralyzed subjects (one paraplegic and two tetraplegic) increased leg circumference and vastus lateralis cross-sectional area in subjects undergoing cycling artificially induced by functional electrical stimulation. In contrast, the claimed invention requires that the administration of a β_2 agonist is effective to increase locomotor function as well as neuromuscular strength. Murphy et al. do not teach that administration of salbutamol increases locomotor function. In addition, even though Murphy et al. teach that their procedure causes an increase in leg circumference, they indicate that "quadriceps muscle contractile function was not modified" (Results section of Abstract), which teaches away from the subject invention. In addition, an increase in locomotor function is not "necessarily present" in the teachings of Murphy et al. since their subjects are paralyzed and cycling was artificially induced by functional electrical stimulation. Murphy et al. note that the effects of β_2 agonists on muscle mass can be observed in denervated muscles (see last paragraph of Discussion on page 1267 in Murphy et al.) In contrast, in the instant invention, β_2 agonists are used to reduce spinal cord injury-induced loss of spinal cord tissue and prevent resulting paralysis and loss of locomotor function (see specification, e.g. page 14, line 10-21, and page 16, lines 1-17).

Vaidyabathan et al. teach the use of salbutamol to treat penile erection that arose reflexively during cystoscopy in two patients with cervical spinal cord injury (tetraplegics). Salbutamol was also used to treat an increase in blood pressure that occurred during autonomic dysreflexia in one of these patients. Vaidyabathan et al. do not teach that administration of salbutamol is effective to increase locomotor function and neuromuscular strength, nor is such teaching "necessarily present" in Vaidyabathan et al. since the subjects were paralyzed.

In addition, the dose range of 5-20 microgram per subject taught in Vaidyabathan et al. does not meet the limitation for an average 70 kg subject of 0.5 μg/kg as required in claim 1.

Furthermore, in regard to the rejections of claims 2, 3, 38, and 39, it is respectfully noted that claims 2, 3, 38 and 39 recite specific β_2 agonists and that none of claims 2, 3, 38 and 39 recite "salbutamol."

Still further, in regard to the rejections of claims 8, 10, 37-41, and 44-46, it is respectfully noted that all of these claims require that the subject have a "spinal cord contusion to the lower thoracic spine." [Emphasis added.] In contrast, the subjects in Vaidyabathan et al. are tetraplegics with injuries in the cervical spinal cord (C5/6 and C3/4). Similarly, in Murphy et al., two subject had cervical spinal injury (C6-C7 and C7-C8), while one subject was injured in the upper half of the thoracic spinal cord at level Th4 (see Table 1 in Murphy et al.).

Thus, the cited references do not expressly anticipate the claims of the subject application. In addition, as discussed above, the claimed invention is not "necessarily present" in the cited references. Furthermore, the cited references do not enable and describe applicants' claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the art, as required by *In re Paulsen*, supra.

Accordingly, in view of the above remarks, applicants respectfully request that the Examiner reconsider and withdraw these rejections.

Rejections under 35 U.S.C. §103(a)

Claim 10 is rejected under 35 U.S.C. §103(a) as not patentable over Murphy et al. (Arch. Phys. Med. Rehabil. 80(10): 1264-67, 1999), as applied to claims 1-3, 5, 8, 37-39 and 41-44 above.

Applicants maintain that claim 37 and 41 are patentable over Murphy et al. for reasons discussed hereinabove and that claim 10, which depends from and further limits, claims 37 and 41, is likewise therefore patentable over Murphy et al.

Accordingly, in view of the above remarks, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Allowable Subject Matter

The Examiner indicated that claims 4, 40, 45, and 46 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants thank the Examiner for this indication of allowable subject matter. Applicants have hereinabove rewritten claims 4 and 40 in independent format to include all the limitations of the base claim. Claims 45 and 46 depend on allowable Claim 40.

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CONCLUSIONS

In light of the above discussion, applicants respectfully request that the Examiner reconsider and withdraw the rejections set forth in the December 3, 2003 Office Action and earnestly solicit passage of the pending claims to allowance.

A check is enclosed for $184.00 to cover the following fees for a small entity: the $55.00 fee for a one month extension of time, and the $129.00 fee for filing three independent claims in excess of the 4 previously paid for (3 x $43.00 per excess independent claim). No other fee is deemed necessary in connection with the filing of this Amendment. However, if any unanticipated payment is required to maintain the pendency of this application, authorization is given to withdraw the amount of any such fee from Deposit Account No. 01-1785. Overpayments may also be credited to Deposit Account No. 01-1785.

Respectfully submitted,

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March 30, 2004

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